REMARKS/ARGUMENTS

Claims 1-15 are active. The claims have been amended for clarity and to conform to U.S. practice. New claims 8-15 find support in the original claims. No new matter has been introduced. Favorable consideration of these amendments and allowance of the case are respectfully requested.

Lack of Unity/Restriction/Election

The Applicants previously elected with traverse for examination purposes the species ***rocR*** as a *Bacillus subtilis* gene. The species ***slr*** and ***sigL*** have been rejoined. The claims are not directed to these genes *per se* so the Applicants construe this requirement within the context of the invention as referring to a recombinant microorganism in which *rocR*, *slr*, or *sigL* (or their equivalents) have been deleted or knocked-out. The requirement has been made FINAL. The Applicants point out that the Office has provided no reasoning as to why microorganisms sharing a functional ability to express a heterologous protein or polypeptide and other significant biological features associated with this ability are patentably distinct. Therefore, it is the Applicants' understanding that additional species will be rejoined and examined upon an indication of allowability for a generic claim reading on the elected species. The Applicants also respectfully request that claims which depend from or otherwise include all the limitations of an allowed elected claim, be rejoined upon an indication of allowability for the elected claim, see MPEP 821.04.

Objection--Specification

The specification was objected to as containing an active hyperlink. This objection is moot in view of the inactivation of the link.

Objection--Claim

Claim 7 was objected to as being improperly multiple dependent. This objection is moot in view of the revision of claim 7 to depend from claim 1.

Rejection—35 U.S.C. §102

Claims 1-4 and 7 were rejected under 35 U.S.C. §102(b) as being anticipated by Ferrari, et al., WO 03/083125. This rejection is moot in view of the amendment of independent claim 1 to delete the term "*slr*". Ferrari is directed to a method of producing a secreted protein by using recombinant *B. subtilis* comprising a deletion of *slr* and was not relied upon for teaching the other deletions or knock-outs required by claim 1.

Rejection—35 U.S.C. §103(a)

Claims 1-7 were rejected under 35 U.S.C. §103(a) as being unpatentable over Ferrari, et al., WO 03/083125, in view of Gardan, et al., Mol. Microbiol. 24:825 and Hakamada, et al., Biosci. Biotechnol. Biochem. 64:2281. This rejection is also moot in view of the amendment of claim 1 since Ferrari was not relied upon for teaching deletions or knock-outs of the genes now recited by claim 1 (including *rocR* and *sigL*) which no longer include *slr*. Ferrari is non-analogous art which does not teach deleting *rocR* or *sigL* as indicated at the bottom of page 4 of the OA.

Gardan did not suggest or provide a reasonable expectation of success for the invention because the skilled artisan would have expected that inactivation of *rocR* would reduce arginine import by negatively regulating arginine permeases RocCE, leading to reduced protein production due to reductions of the amino acid arginine in the cell necessary for protein synthesis. As described by Gardan (cited in rejection) and Belitsky (attached), it

has been well known in the art that RocR positively regulates the rocABC and rocDEF operons, see page 825, first full paragraph and Fig. 1B of Gardan, and page 10290, left col., 2nd paragraph of Belitsky. It was also well known that rocCE are arginine permeases involved with arginine import, see page 825, first full paragraph of Gardan and Fig. 1 of Belitsky.

Similarly, SigL regulates rocABC and rocDEF operons, see the abstract of Gardan, and *sigL* mutants cannot grow when arginine, ornithine, isoleucine, or valine are the sole nitrogen sources, see Debarbouille, et al., abstract (attached).

Second, as disclosed by Gardan and Belitsky, it was well known that RocA, RocD and RocF contributed to arginine metabolism, see Fig. 1A in Gardan and Fig.1 of Belitski. RocA, RocD and RocF have been known as enzymes relating to the production of glutamate from arginine in microorganisms. Based on this well known information, one of skill in the art would have expected that inactivating RocADF would have reduced the conversion of arginine into glutamate and thus cause the accumulation of arginine transported into the cell by the function of arginine permease RocCE.

However, since RocR is a positive regulator of RocCE (arginine permeases), when inhibiting RocR the ordinary artisan would have expected decreased import of arginine into the cell due to inactivation of RocCE. Therefore, the ordinary artisan would have expected that the arginine level in the bacterial cell would be decreased and would not have expected the increased productivity of heterologous proteins expressed by the claimed recombinant microorganisms.

Hakamada was cited in regard to the regulation sequence, but does not disclose the elements of the invention missing from the other references.

In view of the above, this rejection cannot be sustained in view of the amendments above and the lack of a suggestion or reasonable expectation of success for the superior protein expression provided by the claimed recombinant microorganisms.

Conclusion

This application presents allowable subject matter and the Examiner is respectfully requested to pass it to issue. The Examiner is kindly invited to contact the undersigned should a further discussion of the issues or claims be helpful.

Respectfully submitted,

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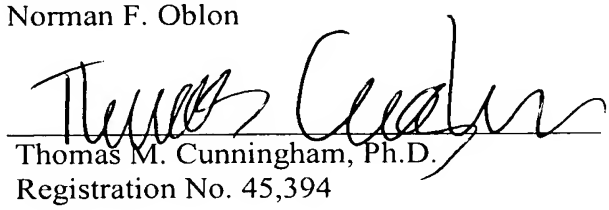

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